ForPatients
by Roche

Breast Cancer

A phase II study evaluating the efficacy and safety of inavolisib plus ribociclib plus fulvestrant versus placebo plus ribociclib plus fulvestrant in patients with advanced breast cancer

A Phase II Study Evaluating the Efficacy and Safety of Inavolisib Plus Ribociclib Plus Fulvestrant Versus Placebo Plus Ribociclib Plus Fulvestrant in Participants With Advanced Breast Cancer

Trial Status	Trial Runs In	Trial Identifier
Not yet recruiting	1 Country	NCT07405801 2025-523013-28-00 CO46274

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase II, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Inavolisib Plus Ribociclib Plus Fulvestrant Versus Placebo Plus Ribociclib Plus Fulvestrant in Patients With Endocrine- Resistant Hormone-Receptor-Positive, HER2-Negative Advanced Breast Cancer With Chromosome 8P Loss and Without a PIK3CA Mutation

Trial Summary:

A study to evaluate the efficacy and safety of triplet combination of inavolisib plus ribociclib and fulvestrant versus placebo plus ribociclib and fulvestrant in the first-line setting in participants with endocrine-therapy-resistant hormone receptor (HR)-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC) with chromosome 8p loss (chr8p loss) and without PIK3CA mutation.

Hoffmann-La Roche Sponsor	**Phase 2** Phase

NCT07405801 2025-523013-28-00 CO46274
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

Hormone receptor-positive (HR+) and human epidermal growth factor receptor 2-negative (HER2-) breast cancer is a type of cancer that starts in the breast. It is made up of cells that have extra hormone receptors but not extra HER2 receptors. These cells can grow more quickly than healthy cells because of the hormones, estrogen and progesterone. Sometimes, the cancer stops responding to hormone treatment (endocrine resistant). When it spreads beyond the breast and nearby lymph nodes and goes to other parts of the body, it is called advanced breast cancer. Some breast cancers are missing part of their genetic material called chromosome 8p (chr8p). These cancers are usually harder to treat because the loss of chr8p makes cancer cells resistant to standard treatments. Better treatment options are needed for people with this type of advanced breast cancer.

This study is testing a medicine called inavolisib, combined with standard treatment (ribociclib plus fulvestrant) in breast cancer that has the loss of ch8p. Inavolisib is currently approved for treatment of HR+, HER2- advanced breast cancer with *PIK3CA* mutation.

At this time, inavolisib is considered an experimental medicine in all other types of breast cancers. This means health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have not approved inavolisib for the treatment of HR+, HER2- advanced breast cancer with loss of ch8p.

This study aims to compare the effects of adding inavolisib to ribociclib plus fulvestrant (standard of care) versus adding a non-active medicine (placebo) to ribociclib and fulvestrant, in people with HR+, HER2- advanced breast cancer with loss of ch8p without *PIK3CA* mutation.

2. Who can take part in the study?

People (males / females) of 18 years and older with HR+, HER2- breast cancer that has spread to nearby tissues or other organs, and is no longer responding to hormone treatment, can take part in the study if their cancer shows a loss of ch8p and does not have a *PIK3CA* mutation.

People may not be able to take part in this study if they have metaplastic breast cancer, a rare type of breast cancer. People may also be excluded if they have certain other medical conditions, such as diabetes, chronic infections, certain autoimmune disorders, or if they are unable to swallow pills. People who are pregnant, trying to get pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

People will be screened to check if they are able to participate in the study. There will be an optional pre-screening step to check whether each potential participant’s tumor has a

‘chr8p loss’ and does not have a change in the *PIK3CA* gene. The screening period will take place from 28 days before the start of treatment.

Everyone who joins this study will be randomly split up into 2 groups (like flipping a coin). One group will be given inavolisib and ribociclib (both as tablets to be swallowed every day) plus fulvestrant, which is an injection into a muscle given twice in the first month and then once a month after that. The other group will receive placebo and ribociclib (both as tablets every day) plus fulvestrant (given as an injection into a muscle twice in the first month and then once a month after that).

Participants have an equal chance of being placed in either group.

This is a ‘placebo-controlled’ study. This means that participants are put in a group that will receive an experimental medicine or a group that will receive ‘placebo’ (a medicine that contains no active ingredients but looks the same and is taken in the same way as the study medicine). Comparing results from the different groups helps researchers know if any changes seen result from the study medicine or occur by chance.

This is a double-blinded study. This means that neither the participants in the study nor the team running it will know which treatment is being given until the study is over. This is done to make sure that the results of the treatment are not affected by what people expected from the received treatment. However, the study doctor can find out which group the participant is in if the participant’s safety is at risk.

During this study, the study doctor will see participants every week during the first month, and then twice during the next two months, after which visits will be once per month plus an interim telephone call while they are receiving study treatment. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have a follow-up visit 1 month after completing the study treatment, during which the study doctor will check on the participant’s well being. Participants with high blood sugar levels at the 1 month follow-up after the end of study treatment will have additional follow-up visits every month for up to 3 months. Total time of participation in the study will range from 1 day to more than 2 years. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main results measured in the study to assess if the medicine has worked are how many participants have a reduction of their cancer after treatment. Other key results measured in the study include:

- How long participants live without their cancer getting worse
- How long participants live

- How much time there is between the participant's cancer first responding to treatment and the cancer getting worse.
- The number of participants whose tumours shrink or stay the same for at least 6 months with study treatment
- The number and seriousness of unwanted effects

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.

It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study medicines Participants may have unwanted effects of the medicines used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Participants will be told about the known unwanted effects of inavolisib, ribociclib, and fulvestrant and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects of inavolisib include a high level of sugar in the blood, feeling tired or weak, loose watery [and more frequent] stools, wanting to throw up, and swelling or sores in the mouth or lips. Known unwanted effects of ribociclib include infections, low levels of white blood cells, feeling less hungry than usual, loose watery [and more frequent] stools, wanting to throw up, throwing up, and belly pain. Known unwanted effects of fulvestrant include joint pain, muscle and bone pain, skin rash, wanting to throw up, allergic reactions, and abnormal liver function blood-test results.

Known unwanted effects of an injection into a muscle include soreness, swelling, or reaction on the skin where it has been pricked with a needle to give a treatment.

The study medicines may be harmful to an unborn baby. Women and men (both study participants and their partners) must take precautions to avoid exposing an unborn baby to the study treatment.

Inclusion Criteria:

- Women or men with histologically or cytologically confirmed carcinoma of the breast that is locally advanced or metastatic and is not amenable to surgical or radiation therapy with curative intent

- Documented estrogen receptor (ER)-positive and/or progesterone receptor (PR)-positive tumor according to American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines, defined as >=1% of tumor cells stained positive based on the most recent tumor biopsy and assessed locally (Allison et al. 2020)
- Participants must not have received any prior systemic therapy for locally advanced unresectable or metastatic breast cancer (mBC) and must have progressed during adjuvant endocrine-based treatment or within 12 months after completing adjuvant endocrine-based therapy with an aromatase inhibitor or tamoxifen
- Confirmed biomarker eligibility as documented through central laboratory testing of a tumor tissue sample documenting both the lack of a phosphatidylinositol-4,5-biphosphate 3-kinase catalytic subunit alpha gene (PIK3CA) mutation and the presence of heterozygous loss of chromosome 8p (i.e., PIK3CAnmd and chr8p loss)
- Measurable disease per Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1)

Exclusion Criteria:

- Metaplastic breast cancer
- Radiotherapy within 2 weeks before randomization
- Appropriate for treatment with cytotoxic chemotherapy at time of entry into the study, as per national or local treatment guidelines (e.g., participants with visceral crisis)
- Type 2 diabetes requiring ongoing systemic treatment at the time of study entry; or any history of Type 1 diabetes
- Known and untreated, or active Central nervous system (CNS) metastases (progressing or requiring anticonvulsants or corticosteroids for symptomatic control). Participants with a history of treated CNS metastases are eligible
- Any history of leptomeningeal disease or carcinomatous meningitis